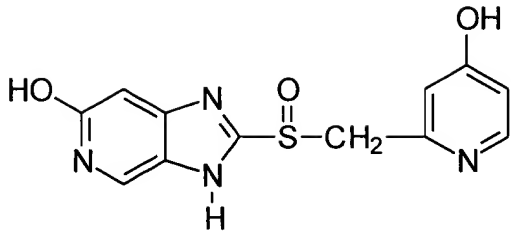

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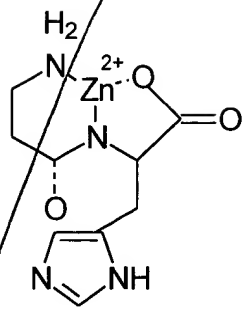

III

and

- at least one pharmaceutically acceptable excipient selected from the group which includes: a binder, an alkaline reaction compound, a surface-active agent, a filling material and a disintegrating-swelling excipient; and

c) a gastro-resistant outer coating on the layer of (b), wherein said gastro-resistant outer coating is made from a solution which includes:

- an enteric coating polymer; and

- at least one excipient chosen from the group which includes: a plasticizer, a surface-active agent, a pigment and a lubricant.

REMARKS

The Examiner is thanked for the many courtesies extended to Applicant's undersigned attorney during the telephone interview of October 4, 2001.

During the telephone interview, Applicant's undersigned attorney provided the Examiner with some background regarding the omeprazole matters and in particular indicated that omeprazole is an acid sensitive compound which can, when contacted by hydrogen ions, undergo certain transformations which, from a pharmaceutical point of view, impact on the shelf life of the product. In particular, it was pointed out many of the commonly used outer enteric coating

layers, such as the Eudragit® coatings, contain acids or acid derivatives which can provide a source of hydrogen ions. When these hydrogen ions diffuse and contact the omeprazole in the formulation, the above-mentioned transformations can occur. In particular, Applicant's attorney pointed out that the Lövgren reference provided a formulation which was specifically designed to avoid this problem. In Lövgren, as discussed below, the problem is addressed by the use of a separating layer and/or an alkaline reacting compounds which presumably would tie up, or neutralize, any free hydrogen ions.

In contrast, the present invention relates to a composition where there is no separating layer. As defined in claim 1, the now claimed composition has an inert nucleus, a soluble active coating layer which contains the active ingredient such omeprazole, and a gastro-resistant outer coating that coats that layer.

In the Office Action of August 3, 2001, the Examiner acknowledged the previously submitted arguments which are set forth below but pointed out that the use of the transitional language "comprising" left the claim open ended. During the interview, the change of the transitional phrase from "comprising" to "consisting essentially of" was discussed. The Examiner indicated at that time that she believed such a change would distinguish the claimed subject matter over the art of record.

Claims 1-4, 6-13, 15, 16 and 18-34 were rejected under 35 U.S.C.103 as unpatentable over European Patent Application 519144 to Tanberk et al. (Tanberk). Claims 1-4, 6-13, 15, 16, and 18-34 were rejected under 35 U.S.C. 103(a) as unpatentable over European Application 773025 to Ballester Rodes et al. (Ballester Rodes). Claims 1-13 and 15-34 were rejected under 35 U.S.C. 103(a) as unpatentable over Tanberk or Ballester Rodes in view of European Patent

Specification 244380 to Lövgren et al. (Lövgren). It is submitted these rejections were improper and should be withdrawn.

The Examiner states that in each of Tanberk and Ballester Rodes, an inert core is coated with a layer of omeprazole or the benzimidazole compound followed by another coating of a water soluble layer or protective coating. The Examiner candidly admits that in each of Tanberk and Ballester Rodes, the enteric coating is the third layer which is applied over the protective layer. The protective layer has been coated over the layer containing the active ingredient and that active ingredient containing layer has been coated on to the inert sugar or starch core.

As also admitted by the Examiner, the present invention is directed to a pharmaceutical composition wherein an inert nucleus is coated by a soluble layer having the active ingredient or a layer which disintegrates rapidly in water and that active ingredient containing layer is in turn coated by the outer or gastro-resistant outer coating. Thus, as recognized by the Examiner, the now claimed invention recites a composition with a two layer coating rather than a three layer coating and Tanberk and Ballester Rodes each disclose a three layer coating.

The Examiner asserts that the product and process taught by each of Tanberk and Ballester Rodes render the now claimed subject matter obvious because one of ordinary skill in the art would have been motivated to use the teachings of Tanberk or Ballester Rodes to create a successful coated particle pharmaceutical formulation with the expected result of having a successful antiulcer formulation and thus the invention as a whole would have been *prima facie* obvious.

It is respectfully submitted that the rejections are in error.

The references provide no motivation to alter the formulations or pellet structure disclosed therein. To the contrary, each of the references alone and in combination teaches away from the now claimed invention.

There is no suggestion in either of Tanberk or Ballester Rodes that a two-layer structure could be employed when the active ingredient is omeprazole or a similar benzimidazol.

The Examiner's explanation does not provide motivation and does not establish on the record how the cited references show or suggest the now claimed invention. What in any of the references provides motivation to remove one of the layers that is required in each of those references. In effect, the Examiner has modified each of the references. However, without art provided motivation for such a modification, this is improper. See, In re Hummer, 113 U.S.P.Q. 66, 69 (CCPA 1957)(Prior patent is reference only for what it clearly shows or discloses or suggests; it is improper use of patent to modify its structure to one which it does not suggest).

There is no disclosure in any of the references that suggests that a two-layer structure would be successful. In this regard, the Examiner is in effect ignoring what each of the references considers to be an essential ingredient or feature of the respective invention disclosed therein. Thus, the Examiner has improperly attempted to modify those references and in doing so has postulated a formulation or structure which would undermine the very purpose of the invention disclosed in each of those references. This is again improper under 35 U.S.C. 103 see In re Ratti 123 U.S.PQ. 349, 352 (CCPA 1959).

The combination of the Lövgren reference with either Tanberk or Ballester Rodes does not overcome the teachings of either of the references which discloses a three-layer structure.

In Lövgren, the active ingredient can be in the core. However, it is clear from Lövgren that there must be a separating layer between the active ingredient (omeprazole) and the outer

enteric coating layer. The purpose of the separating layer is to avoid contact of the acid labile active ingredient with the enteric coating layer which generally is composed of one or acidic-like materials. Lövgren teaches that the alkaline containing separating layer between the active ingredient and the enteric coating layer will protect the active ingredient from the acidic properties of the enteric coating or outer layer. Thus, Lövgren also teaches away from the now claimed subject matter.

In view of the foregoing, reconsideration and allowance of the application with claims 1-13 and 15-34 are earnestly solicited.

Respectfully submitted,
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Dated: October 9, 2001

Version with Markings to Show Changes

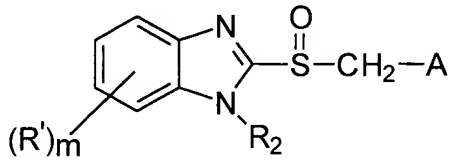
In the Claims:

1. (Twice amended) An oral pharmaceutical preparation [comprising] consisting essentially of:

a) an inert nucleus;

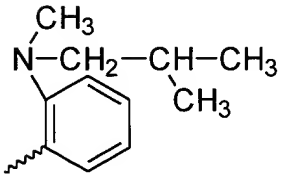
b) a soluble active layer or layer which disintegrates rapidly in water, made from a single aqueous or hydroalcoholic solution-suspension which comprises:

- an active ingredient of anti-ulcer activity of general formula I

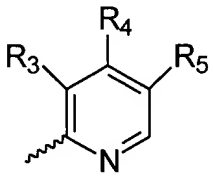


wherein:

A is:



or



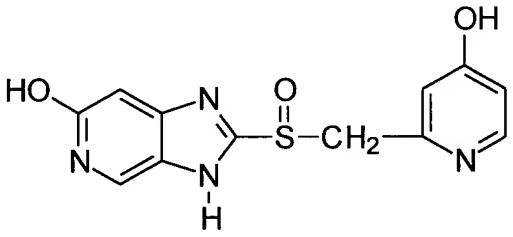
in which: R^3 and R^5 are the same or different, and may be hydrogen, alkyl, alkoxy, or alkoxyalkoxy;

R^4 is hydrogen, alkyl, alkoxy which can optionally be fluorated, alkoxyalkoxy, or alkoxycycloalkyl;

R^1 is hydrogen, alkyl, halogen, cyano, carboxy, carboalkoxy, carboalkoxyalkyl, carbamoyl, carbamoylalkyl, hydroxy, alkoxy, hydroxyalkyl, trifluoromethyl, acyl, carbamoyloxy, nitro, acyloxy, aryl, aryloxy, alkylthio or alkylsulphinyl;

R^2 is hydrogen, alkyl, acyl, carboalkoxy, carbamoyl, alkylcarbamoyl, dialkylcarbamoyl, alkylcarbonilmethyl, alkoxycarbonilmethyl or alkylsulfonil; and, m is a whole number from 0 to 4;

or of formula II or III,



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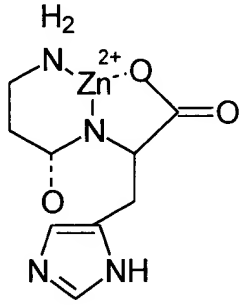

III

and

- at least one pharmaceutically acceptable excipient selected from the group which includes: a binder, an alkaline reaction compound, a surface-active agent, a filling material and a disintegrating-swelling excipient; and

c) a gastro-resistant outer coating on the layer of (b), wherein said gastro-resistant [out] <u>outer</u> coating is made from a solution which includes:

- an enteric coating polymer; and
- at least one excipient chosen from the group which includes: a plasticizer, a surface-active agent, a pigment and a lubricant.